

## REMARKS

### Claim Rejections

Claims 101, 104-106, and 111-125 are pending in the present case.

The Examiner has maintained the a number of rejections. For clarity, these rejections are summarized below in the order in which they are addressed:

1. Claims 101, 104, 111-117, and 123-125 stand rejected as being allegedly being anticipated under 35 U.S.C. § 102(b) by Harrington, *et al.*, EMBO Journal vol 13:1235-1246 (1994), hereinafter "Harrington I;"
2. Claims 101, 104, 111-117, and 123-125 stand rejected as being allegedly being anticipated under 35 U.S.C. § 102(b) by Harrington, *et al.*, J. Biol. Chem 270:4503-4508 (1995), hereinafter "Harrington II;"
3. Claims 105-106 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Dahlberg, *et al.*, patent publication WO 94/29482, hereinafter "Dahlberg;"
4. Claims 105-106 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Dahlberg;
5. Claims 105-106, 118-119 and 122 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Urdea;
6. Claims 105-106, 118-119 and 122 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Urdea;
7. Claims 120-121 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Corey;
8. Claims 120-121 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Corey;
9. Claims 101-106 and 111-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 11/031,487, hereinafter "'487;"

10. Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '487 in view of Corey;
11. Claims 101-106 and 111-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 10/754,408, hereinafter "'408;"
12. Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '408 in view of Corey.

### **The Claims Are Not Anticipated**

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d. 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). As explained in more detail below, none of the references cited sets forth each and every element of the rejected claims.

1-2. Claims 101, 104, 111-117, and 123-125 stand rejected as being allegedly being anticipated under 35 U.S.C. § 102(b) by Harrington, *et al.*, EMBO Journal vol 13:1235-1246 (1994), hereinafter "Harrington I. These claims also stand rejected as being allegedly being anticipated under 35 U.S.C. § 102(b) by Harrington, *et al.*, J. Biol. Chem 270:4503-4508 (1995), hereinafter "Harrington II;"

The Examiner maintains these rejections from the Office Action mailed on November 8, 2005. In making these rejections, the Examiner maintains that a "thermostable" nuclease of the instant application is interpreted to be a "nuclease that is stable at a specific temperature." The Examiner asserts that the specification does not define the term to be limited to stability at any particular temperature (Office Action, page 3). Applicants disagree for the following reasons:

- a) The Examiner fails to provide evidence that the meaning used as the basis for these rejections is the "plain meaning" as understood by those of skill in the art;

- b) Applicants are entitled to be their own lexicographers by providing a definition of "thermostable" as applied to a nuclease in the specification;
- c) A definition for the term "thermostable" as applied to a nuclease is clearly set forth in the specification.

The Examiner asserts that the thermostable nuclease of the claims is a "nuclease that is stable at a specific temperature." The Examiner further asserts that the specification does not define the term to be limited to stability at any particular temperature (Office Action, page 3). For the reasons recited below, Applicants disagree that the specification does not provide a specific definition for the term. However, even if the claim is interpreted under a "broadest reasonable interpretation" standard, the Examiner has provided **no** support for interpreting a "thermostable" nuclease as a nuclease that is "stable at a specific temperature." The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. (MPEP § 2111, citing *In re Cortright*, 165 F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999)). The Examiner has provided no evidence that this interpretation is consistent with the interpretation that those of skill in the art would reach.

Similarly, no support is provided for asserting that the Examiner's definition is consistent with a plain meaning for this term. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, *i.e.*, as of the effective filing date of the patent application." (MPEP § 2111.01, citing *Phillips v. AWH Corp.*, F.3d 75, USPQ2d 1321 (Fed. Cir. 2005) (en banc), emphasis added). The Examiner has provided no evidence related to the asserted plain meaning (*i.e.*, the meaning this term would have to a person of ordinary skill in the art) of this term. As such, there is no basis for the Examiner's position that the thermostable nuclease of the claims is a "nuclease that is stable at a specific temperature."

Even if this is taken for the "plain meaning" of the term "thermostable," (and Applicants do not agree that it is), Applicants are entitled to be their own lexicographers and "may rebut the presumption that claim terms are to be given their ordinary and

customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s)" (MPEP § 2111.01, quoting *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994). Furthermore, "[w]here an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim." (MPEP § 2111.01, citing *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999))

Applicants have clearly set forth a definition for the term "thermostable" as applied to a nuclease. As indicated by the capitalized header reading "DEFINITIONS" on page 26, line 22, Applicants have provided a section of the specification devoted to providing definitions for a number of terms used in the specification and claims, with each of these defined terms indicated by the use of quotation marks. The DEFINITIONS section of the specification provides:

The term "thermostable" as used herein in reference to an enzyme, such as a 5' nuclease, indicates that the enzyme is functional or active at an elevated temperature, *i.e.*, at about 55°C or higher.

(Page 32, lines 16-18.)

The statement above is identified as a "definition" within the specification, and a written definition is provided for the term. As noted above, "Where an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim." (MPEP § 2111.01, citing *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999)). Thus, Applicants submit that the Examiner must interpret the recited thermostable nuclease of the instant claims as being a nuclease that is "functional or active at an elevated temperature, *i.e.*, at about 55°C or higher."

Neither Harrington I nor Harrington II teach or recite a thermostable 5' nuclease, *i.e.*, a 5' nuclease that is functional or active at about 55°C or higher. Rather, Harrington I teaches 5' nucleases isolated from mammalian cells and teaches their use at 30°C (see, *e.g.*, page 1245, column 1). Harrington II teaches 5' nucleases isolated from mammalian and yeast cells (see, *e.g.*, 4503, column 2) and teaches their use at 30°C (see, *e.g.*, page

4504, column 1). Neither Harrington I nor Harrington II teach or suggest that the disclosed enzymes have any stability or activity at or above about 55°C. As such, neither Harrington I nor Harrington II teach or suggest the recited combination of the instant claims, of a 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, as recited in Claim 101 and dependent claims.

For the reasons recited above, Applicants submit that neither Harrington I nor Harrington II teach or suggest each and every element set forth in Claims 101, 104, 111-117, and 123-125, and thus does not anticipate these claims. Applicants therefore respectfully request that these rejections be removed.

#### **The Claims Are Not Obvious**

Prima facie obviousness requires 1) a suggestion or motivation in the references or the knowledge generally available to combine or modify the reference teachings; 2) the prior art must teach of a reasonable expectation of success should the suggested combination or modification take place; and 3) the prior art must teach or suggest all the claim limitations. MPEP § 2143. A showing of obviousness will fail if any one of these elements is not met. As explained in more detail below, none of the cited combinations of references cited sets forth each and every element of the rejected claims.

3. Claims 105-106 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Dahlberg.

Claims 105 and 106 both depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington I does anticipate Claim 101 because Harrington I does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Dahlberg fails to overcome this deficiency. Dahlberg does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined

regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Dahlberg teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Harrington I and Dahlberg does not teach or suggest all the limitations of Claims 105 and 106, and the cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.

4. Claims 105-106 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Dahlberg.

Claims 105 and 106 both depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington II does anticipate Claim 101 because Harrington II does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Dahlberg fails to overcome this deficiency. Dahlberg does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Dahlberg teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Harrington II and Dahlberg does not teach or suggest all the limitations of Claims 105 and 106, and the cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.

5. Claims 105-106, 118-119 and 122 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Urdea.

Claims 105-106, 118-119 and 122 depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington I does anticipate Claim 101 because Harrington I does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Urdea fails to overcome this deficiency. Urdea teaches the cleavage of a labeled oligonucleotide on a solid support using, *e.g.*, a restriction enzyme. Urdea does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Urdea teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing *prima facie* obviousness have been met, Applicants submit that the combination of Harrington I and Urdea does not teach or suggest all the limitations of Claims 105-106, 118-119 and 122, and cited art therefore fails to establish *prima facie* obviousness. Applicants respectfully request that this rejection be removed.

6. Claims 105-106, 118-119 and 122 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Urdea.

Claims 105-106, 118-119 and 122 depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington II does anticipate Claim 101 because Harrington II does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Urdea fails to overcome this deficiency. Urdea teaches the cleavage of a labeled oligonucleotide on a solid support using, *e.g.*, a restriction enzyme. Urdea

does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Urdea teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Harrington II and Urdea does not teach or suggest all the limitations of Claims 105-106, 118-119 and 122, and the cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.

7. Claims 120-121 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington I in view of Corey.

Claims 120 and 121 depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington I does anticipate Claim 101 because Harrington I does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Corey fails to overcome this deficiency. Corey teaches the attachment of a polypeptide to a nucleic acid to enhance hybridization. Corey does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Corey teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Harrington I and Corey does not teach or suggest all the limitations of Claims 120 and 121, and cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.



8. Claims 120-121 stand rejected as being allegedly being unpatentable under 35 U.S.C. § 103(a) over Harrington II in view of Corey.

Claims 120 and 121 depend from Claim 101 and incorporate each recited element of Claim 101. For the reasons recited above, Applicants submit that Harrington II does anticipate Claim 101 because Harrington II does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity. Corey fails to overcome this deficiency. Corey teaches the attachment of a polypeptide to a nucleic acid to enhance hybridization. Corey does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease lacking synthetic activity, nor does Corey teach the cleavage of such overlapping structures with a thermostable 5' nuclease lacking synthetic activity. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Harrington II and Corey does not teach or suggest all the limitations of Claims 120 and 121, and cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.

**Obviousness-type Double Patenting Rejections.**

The Examiner has made the following obviousness-type double patenting rejections:

9. Claims 101-106 and 111-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '487.

10. Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '487 in view of Corey.


11. Claims 101-106 and 111-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '408.
12. Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '408 in view of Corey.

Applicants respectfully submit that all other grounds for rejection in the instant application have been addressed. The two applications cited by the Examiner in making the above-recited obviousness-type double patenting rejections, co-pending Application Ser. No. 10/754,408, filed 01/09/2004 and co-pending Application Ser. No. 11/031,487, filed 01/07/2005, are both later filed than the instant application (which was filed 02/12/2002). In accordance with MPEP § 804 I.B.1 procedure regarding provisional double patenting rejections involving earlier and later filed applications, Applicants respectfully request that each of these double patenting rejections be withdrawn from this earlier filed case and that the claims be passed to allowance without terminal disclaimer.

## CONCLUSION

For the reasons set forth above, it is respectfully submitted that all rejections have been addressed and should be removed, and Applicants' claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

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